PTC 785

Sensory information from afferent neurons

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PROGRESS REPORT #2

for the period

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This QPR is being sent to you before it has been reviewed by the staff of the Neural Prosthesis Program.

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I. Objectives of Overall Project

In this newly awarded research contract we will build on the work done in the initial 3-year contract (NO-NS-3-2380). Our aim is to develop and perfect, in an animal model, methods for chronic recording and processing of afferent activity produced by sensory receptors that could yield information about human fingertip contact, grasped object slip, finger position, and grasp force applicable for restoration of motor functions in the paralyzed human hand. The specified contract objectives are:

1. Select recording methods that:
   a. Have the potential of providing safe, reliable recordings in humans for periods of years.
   b. When used in human applications, could provide relatively isolated information from the sensory endings in the thumb pad and in the finger pads of the second and third fingers.
   c. Could, in human applications, provide information from the proprioceptive receptors in the muscles of the hand and wrist.

2. Select an animal model suitable for chronic recording of afferent nerve activity, and give consideration to modeling electrode placement sites for a potential human neural prosthesis application.

3. Fabricate or obtain chronic electrodes and associated cables and percutaneous connectors for chronic recording of sensory afferent activity.
   a. Design electrodes and cables using biocompatible materials that would be suitable for potential future human implants.
   b. Design electrodes and cables with the goal of producing a chronic implant that causes minimal nerve damage.

4. Investigate the possibility of extracting information about contact, grasped object slip, limb position and contact force from chronically recorded neural activity using the animal model and electrodes from parts 2 and 3.
   a. Devise recording, processing, and detection methods to extract this information from recorded neural activity in a restrained animal.
   b. Modify these methods as needed to function in an unrestrained animal and in the presence of stimulation artifacts associated with functional electrical stimulation.
   c. Record activity for periods of at least 6 months and devise functional measures to track any change in neural response over this time.
   d. Evaluate any histological changes in the nerves that occurred over the period of chronic recording and, if possible, correlate these changes to changes in functional response.

5. Cooperate with other investigators in the Neural Prosthesis Program by collaboration and sharing of experimental findings.

II. Summary of Progress in the Second Period

During this reporting period we have made significant progress in developing methods to obtain selective multi-channel ENG recordings. We performed more acute experiments on cats to evaluate new designs of multi-contact nerve cuffs and obtained results that were substantially better than those reported in the literature from similar experiments using more conventional multi-contact cuff designs.

Based on results from these acute experiments, during this reporting period we implanted the first three cats of a new series intended for chronic evaluation of the safety and longevity of multichannel recording devices. Two were implanted with a four-channel Multi-Contact Cuff (MCC) on each of the Median and Ulnar nerves, and one was implanted with four pairs of Longitudinal IntraFasiscular Electrodes (LIFEs) in each of the Median and Ulnar nerves. We periodically monitored compound action potentials (CAPs) under anesthesia to determine the status of the nerves and the recording characteristics of the electrodes. Each animal was instrumented with a stimulating nerve cuff proximal to the elbow. The status of the nerve was monitored by recording a CAP with tripolar, circumferential electrodes located within the MCC itself or by recording a CAP distal to the LIFEs with a standard tripolar recording nerve cuff with circumferential electrodes.

The overall goal is to determine in real time which digits are being stimulated based solely on multiple signals recorded by the MCCs or by the LIFEs implanted on the two main forelimb nerves. To provide selective inputs, we developed two protocols under anesthesia that involve either electrical stimulation of individual digits or mechanical perturbation of individual digits and simultaneous recordings from various nerve electrodes. These protocols were used to collect ENG data from the MCCs and the LIFEs to evaluate the selectivity of the electrode arrays pertaining to the stimulation or perturbation of single digits. A new definition of selectivity was developed and is presented in this report.

III. Details of Progress in the Second Period

A. Background on previous research into selectivity with nerve cuffs

Selective recordings involve the ability to discriminate the source of an input signal from amongst many possible signal sources. A couple of decades ago and again more recently, three different groups have studied the issue of making selective recordings (Lichtenberg and De Luca, 1979; Struijk et al., 1996; Sahin and Durand, 1996). They used similar preparations, electrode arrays and recording methods, but different analysis techniques. All groups have used anesthetized animal preparations with direct electrical stimulation of nerve branches. This preparation provides signal sources that have very little noise contamination due to EMG interference and little natural background activity. Recordings of the resulting compound action potentials are made with nerve cuffs located at sites proximal to the stimulation sites.

However, the type of analysis and the definition of selectivity has varied from group to group. The common definition of selectivity has been some sort of difference in the amplitude of recorded signals. Sahin and Durand (1996) defined selectivity as the difference in normalized signals. Lichtenberg and De Luca (1979) used a statistical

difference to measure selectivity and used more complex mathematical modelling to calculate the centre of electrical activity in the cross section of a nerve. Struijk et al. (1996) used comparisons of ratios of recorded signals to develop a selectivity measure.

In 1979, Lichtenberg and De Luca first studied the question of selective recordings in the sciatic nerve of the rabbit. Six nerve branches - peroneal, plantaris, lateral gastrocnemius, tibial, flexor digitorum longus, and soleus - were stimulated with hook electrodes and recordings were made from five different sites along a 2.3 cm section of the sciatic nerve. The electrode that was used was a nerve cuff 10 mm long and 2.3 mm in diameter, which had slightly smaller cross section than the sciatic nerve and caused a tight fit about the nerve. Eight wires were placed in the cuff with four in each of two transverse planes separated by 2 mm. Circumferential recordings amongst pairs of wires in the same plane were made, as well as recordings between the longitudinal pairs.

To analyze the data, the recordings that were made from each pair of electrodes were first averaged over all of the stimulation trials and then normalized to the maximum recorded amplitude on a given channel at each position for each nerve branch. Duncan's multiple range test was used to indicate significant differences in the means of the normalized amplitudes as a function of the stimulated nerve branch. In both the longitudinal and circumferential studies, the peroneal nerve could be most easily identified from the extensor nerve branches with less selectivity present amongst the other nerve branches. Later, the longitudinal data was used to estimate the centres of electrical activity within a cross section of the nerve. The results of the estimates "correlate[d] reasonably well with anatomical data describing the location of the nerve fibres."

Recently, Struijk and Haugland (1996) also performed their own selective recordings and analysis. They also studied the sciatic nerve of the rabbit, but they only stimulated two branches - the peroneal and tibial nerves. Their nerve cuff was 25 mm long with a 4x2 mm^2 cross sectional area, larger than the typical sciatic nerve at 3x1 mm^2. Twelve electrode contacts were in the cuff with four electrodes in each of three transverse planes separated by 10 mm.

Two recording configurations were used in Struijk et al.'s setup (1996). In the first, a regular tripolar configuration was used in which three electrodes in a longitudinal line were configured so that the outer electrodes were tied together and formed a reference and the centre electrode acted as the signal source. In the second configuration, the reference electrodes from one longitudinal electrode array were tied to the reference electrodes of the other electrode arrays. That is, all of the outer electrodes were connected and only the four inner electrodes were used as signal sources.

In the analysis of the data, a "selectivity ratio" was defined as the ratio of rms amplitudes of the recorded CAPs after stimulation of the peroneal or tibial nerves. A "selectivity indicator" was defined as the square root of the product of the two selectivity ratios. Similar results were found for both recording scenarios, with a selectivity indicator of 1.4 for the first configuration and 1.3 for the second configuration.

Sahin and Durand (1996) also studied selectivity with their own electrode array. They conducted their studies on the hypoglossal nerve of the Beagle dog with a tight fitting nerve cuff that would exclude all fluids from inside the cuff. The cuff was 20 mm long, 2.5 mm in diameter, and had 12 contacts in the walls of the cuff. The electrodes were spaced in three transverse planes with 7 mm separation between the planes. Two recording scenarios were used. In the first, regular tripolar recordings were made along longitudinal sections of the cuff, as in the Struijk and Haugland case, and in the second, contacts on opposite sides of the cuff were shorted together.

To analyze their data, Sahin and Durand first normalized the recorded CAP data at each contact set by the sum of all recordings at each contact set for a given nerve branch. Next, a "selectivity index" was calculated by normalizing the normalized data from the first step by the sum of the normalized recordings of a given nerve branch. The term "selectivity" then refers to the spread in the selectivity indices of a contact set for various fibre subpopulations. The selectivity was found to be better for the second recording scenario. Sahin and Durand's conclusion was that selective recordings are possible, "but the effects are small".

B. Acute experiments with Multi-Contact Cuffs

In the summer of 1996 we performed three acute experiments to test our new multi-contact cuff designs. Although the details differed slightly, the majority of the protocols of the experiments were the same. In each of the experiments, the sciatic nerve of the hindlimb of the cat was exposed and five to eight of its nerve branches were dissected free. These nerve branches included the common peroneal, tibial, lateral gastrocnemius-soleus, medial gastrocnemius, sural, and perforant branch of biceps.

In the first experiment, five nerve branches were teased free and stimulated - the common peroneal, tibial, lateral gastrocnemius-soleus, medial gastrocnemius, and sural nerves. Hook electrodes were used to stimulate each of the nerve branches and recordings were made from each of the contact sets in the nerve cuff that was placed on the sciatic nerve. To make measurements of the compound action potentials, the signals were amplified and then displayed on a digital oscilloscope from which hardcopies of the signals were obtained. Measurements of the signal amplitudes were taken from the paper copies from the oscilloscope and these numbers were used to calculate the selectivity values for the various cuff configurations. The data from the experiment were archived onto FM tape.

A plot of the selectivity of the multi-contact cuff from Acute #1 is shown below. The selectivity indices were calculated by the method presented by Sahin and Durand (1996). The degree of selectivity is shown by the amount of spread of the selectivity indices for a given contact set. If there were no selectivity, then each selectivity index would just be given by 100% divided by the number of stimulated nerve branches; in this case, 20%. In contrast, the spread seen in Figure 1 is quite large.

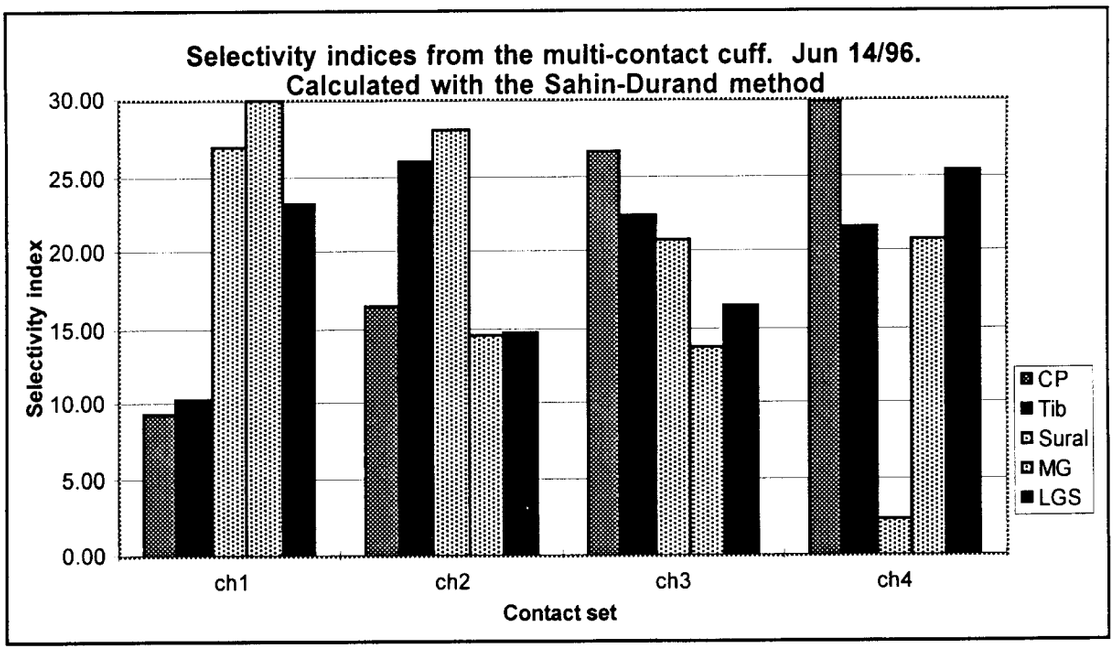


Figure 1: Selectivity indices from Acute #1

We have found that a useful metric to further analyze the results is to calculate the coefficient of variation, the standard deviation divided by the mean, of each of the contact sets and then average all of these values to get the coefficient of variation for the whole nerve cuff. The coefficient of variation analysis removes the variable for average selectivity index for each contact set (i.e. SI = 20 for five stimulated nerves, and SI = 33.3 for three stimulated nerves) and allows for the direct comparison of different experiments with different number of stimulated nerves.

For the data set shown in Fig. 1, the coefficient of variation was found to be 40%. By comparison, the data presented in Sahin and Durand (1996) shows a coefficient of variation of approximately 5% for their first recording scenario and 9% for their second recording scenario (we calculated these values directly from the data published in their paper, which appears in the form of our Fig. 1). This suggests that Sahin and Durand's cuffs obtained relatively low selectivities, or low standard deviation for each contact set, during these recordings. An appropriate question which should be addressed is, what minimum coefficient of variation is necessary for reliable signal separation and identification during repeated recordings?

In our second experiment, a similar surgical protocol was followed, but this time eight sciatic nerve branches were exposed and stimulated. The common peroneal and tibial nerves were each divided into two branches and the perforant branch of biceps was also exposed. This time, stimulating cuffs were implanted onto each of the nerve branches to facilitate stimulation. In this set of experiments, we tested two alternative multi-contact cuff designs to determine which would provide the most selective recordings. We first tested one cuff three times and then a more conventional cuff two times. To test whether or not the selectivity of the cuff was dependent upon its position on the nerve, we rotated the cuff by approximately 45°. The results of the first test are shown in Figure 2, below.

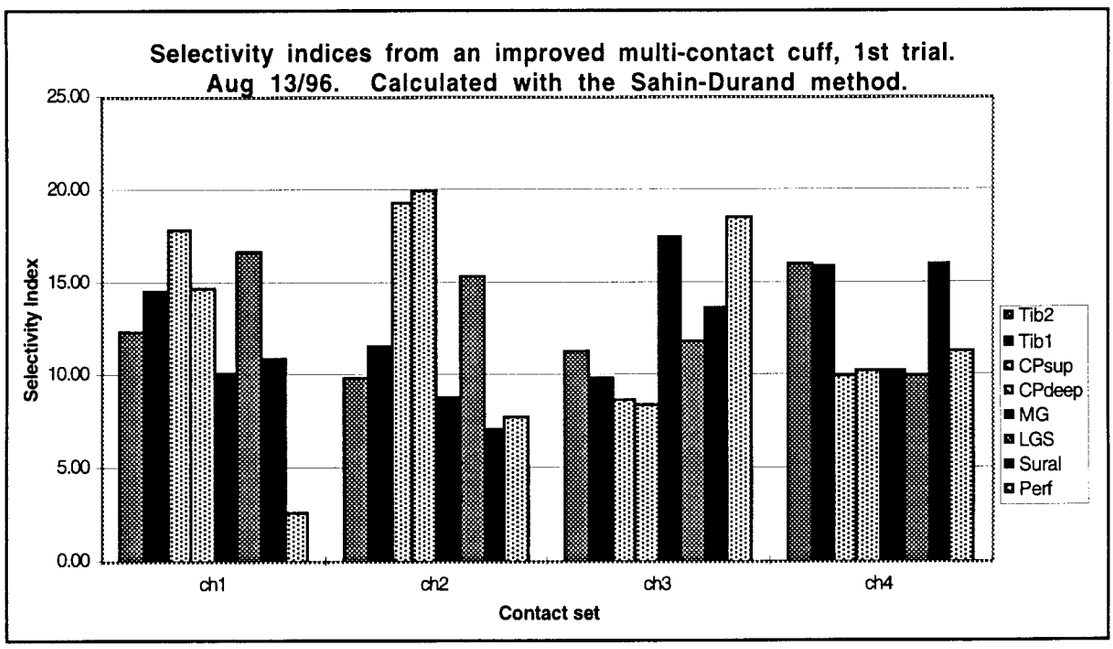


Figure 2: Selectivity indices from the improved multi-contact cuff in Acute #2
The data in this graph have a coefficient of variation of 34%. The coefficient of variation of the three tests had an average of 34%, with a range from 30% to 39%.

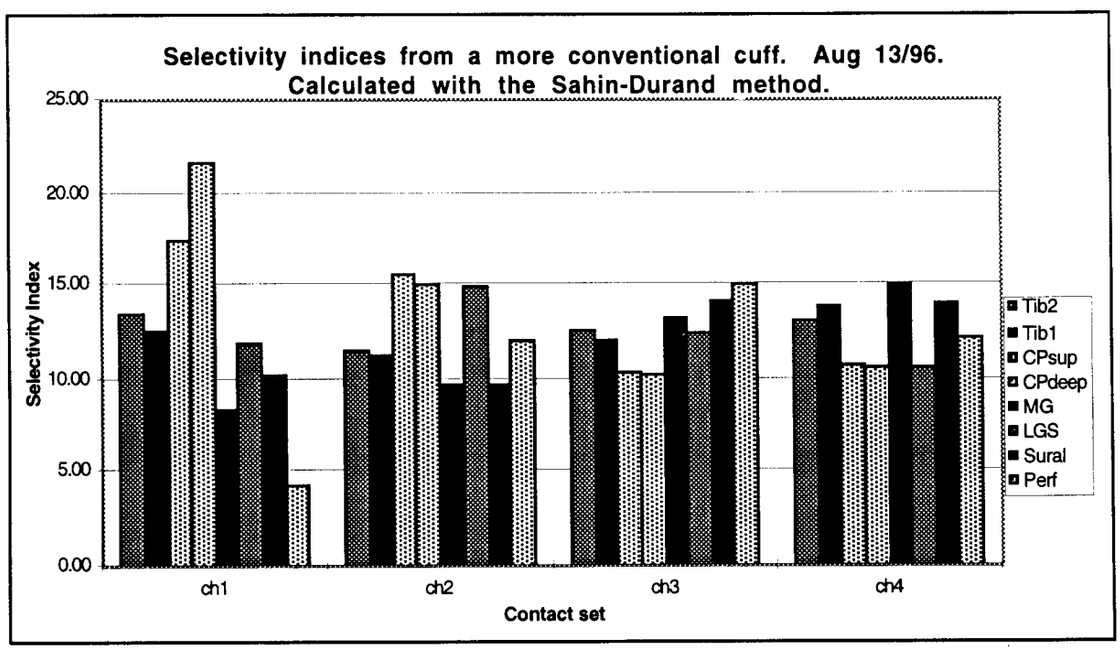
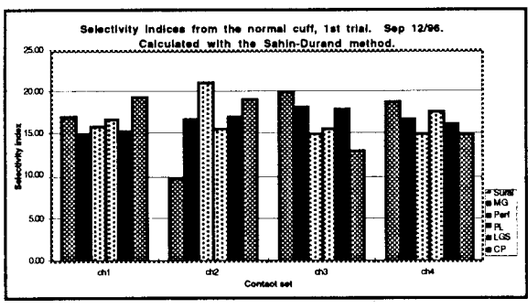
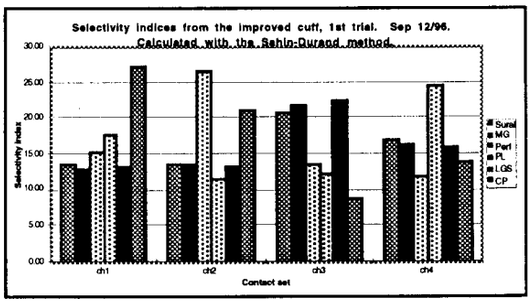


Figure 3: Selectivity indices from a more conventional multi-contact cuff in Acute #2
After finishing the tests with the improved cuff, we tested a more conventional multi-contact cuff. The results of the test are shown in the above graph. This data set has a coefficient of variation of 22%. The average of the two trials was 21% with a range from 21% to 22%.

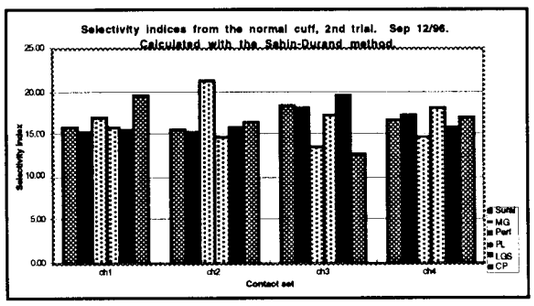
After completing the second experiment, we realized that the results of this comparative study were inconclusive because we could not determine whether or not the improved selectivity was due solely to a better cuff design. We could not rule out that nerve conditions deteriorated over the course of the experiment such that the selectivity diminished with time. So, in a third acute set of experiments we alternated between using a conventional multi-contact cuff and an improved cuff. The first and third tests were performed with the conventional cuff and the second, fourth, and fifth tests were performed with the improved cuff. By setting up the test in this manner we hoped to minimize the potential effects of time on the results of selectivity. The data have been plotted in the following graphs along with the coefficients of variation for each of the data sets.



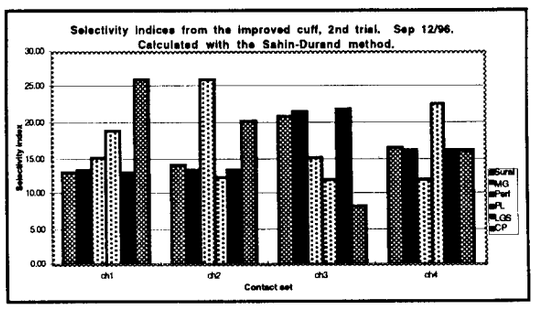
Test 1. Coefficient of variation: 14%



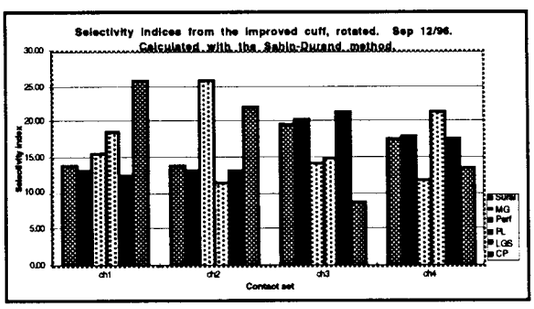
Test 2. Coefficient of variation: 32%



Test 3. Coefficient of variation: 12%



Test 4. Coefficient of variation: 30%



Test 5. Coefficient of variation: 29%

Figure 4: Selectivity indices from Acute #3

One can see from the above figures that the recordings made from the cuffs are reproducible from test to test. For example, in test 2 and 4, which are the data from the improved cuff, contact set one is has the highest selectivity index for the common peroneal nerve, contact set two has the highest selectivity index for the perforant branch of biceps, contact set three is the preferred recording site for the sural and gastrocnemius nerves, and contact set four has the highest selectivity index for the plantaris nerve.

From the results of this experiment, we concluded that the changes that we made to the multi-contact cuff design considerably improved the selectivity of recordings from nerve cuffs. We then decided to proceed with constructing similar cuffs for subsequent chronic implants.

C. Development of a Selectivity Index

1. Rationale for a selectivity index

Although other groups have developed their own methods to calculate selectivity indices, we derived our own definition of a selectivity index that is based in linear algebra. Our selectivity index uses the linear distance between two normalized vectors to give an impression of the level of selectivity of a recording set. The selectivity index for a particular cuff or electrode array provides a single value that is based on the average distance between all pairs of recorded data.

The more selective a recording cuff is, the more likely it is to discriminate recorded neural signals originating from various nerve branches, fascicles, or other stimulus sites. In our method, a selectivity of 100 is the maximum possible and a selectivity of 0 implies that there is no discernible difference between signals arising from any of the sources.

2. Calculating the selectivity of an electrode array

After the multi-contact cuff or electrode array has been implanted and individual signal sources (e.g., stimulated nerve branches or digits) have been identified, the sources are stimulated one by one and recordings of the resulting compound action potentials are made from all of the electrodes in the cuff synchronously.

After the data have been collected, they are arranged as an n-dimensional vector with one vector per stimulated nerve branch. Each element within the vector represents the peak to peak amplitude of a compound signal recorded on one of the contact sets such that the first element in the vector is the data from the first contact set, the second is from the second contact set, and so on.

Initially, the individual elements in the data vectors can have any positive value, however after Euler normalization the sum of the squares of the elements totals 1. This normalization step is applied to all of the data vectors that are obtained from the electrode array after all sources have been stimulated. The reason for normalizing the vectors in this manner is to decrease the dependence on overall source signal strength since nerve branches may have different sizes and their signal amplitudes may fluctuate over time.

To calculate the degree of separation, or selectivity, of the various data vectors, the linear distance between each pair of the vectors is found. To make the resulting intervector distance measures more readable, we have further scaled all distances within the range from 0 (no selectivity) to 100 (maximum possible selectivity).

After all of the vectors have been normalized and the linear distances between all pairs of vectors have been calculated and scaled, the average selectivity of a signal source may be calculated. The average selectivity for a signal source is calculated by averaging the linear distance for one vector to all other vectors. To obtain the overall average selectivity for all signal sources, the aggregate average is taken. In our technique, this is achieved by averaging all of the individual sources' average selectivities to obtain one average selectivity measure that characterizes the multi-contact cuff array's ability to record separable signals from all the sources.

Using the Euler distance method, the following selectivity index values were computed for the acute experiment results shown in Figs. 1 - 4. The data from Fig. 1 had an average selectivity of 37, Fig. 2 had an average selectivity of 28, and Fig. 3 had an average of 14. For the third acute (data shown in Fig. 4a-e), average selectivity indices of 13, 28, 11, 26, and 19 were obtained for the alternating cuff designs. In general, these average selectivity index values showed the same trends as the coefficients of variation produced after applying the Sahin - Durand analysis method.

D. Chronic experiments investigating selectivity

1. Multi-Contact Cuffs

In the first series of chronic multi-contact implants we targeted the median and ulnar nerves as the nerve sources for the multi-contact cuff experiments. We selected these two nerves because they innervate the whole volar aspect of the forepaw of the cat. The median nerve innervates digits I, II, III and IV and the ulnar nerve innervates digits IV and V. To date, we have implanted two cats, NIH 18 and NIH 19.

Each MCC consisted of a 15 mm long standard tripolar cuff that used the closing mechanism reported in previous progress reports and in a recent US patent (Kallesøe et al., 1996). Eight "localized" electrodes were added to the cuff in two radially distributed sets, resulting in four bipolar pairs of electrodes. This distributed electrode placement allowed for recording from four quadrants on the surface of the nerve. Further details about electrode type and localization will not be reported at this time as they are considered proprietary information.

Electrical stimulation of digits to test selectivity

One of the tests for selectivity of the implanted multi-contact nerve cuffs that we have been using is to stimulate the surface of each digit directly with a cuff-like tube that has two stimulating wires sewn into it. During these tests the subject is anesthetized so that there is no EMG activity and little background neural activity. This preparation is therefore similar to previous tests in which nerve branches were stimulated directly, but this time the independent signal sources are individual digits rather than individual nerve branches.

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The analysis that we applied to the collected data is similar to the acute hindlimb experiments except that in the chronic forelimb experiments there were five signal sources and eight contact sets spread over two nerve cuffs. Figure 5 shows an example of the signals recorded on the eight different recording channels when each of the digits was stimulated externally.

As explained above, the peak-to-peak CAP amplitude data that is collected from each contact set forms an element in a data vector for each digit. The vectors are then normalized to have a length of one and then the linear distance between each pair of vectors is calculated and scaled. For the signals shown in Fig. 5 (cat NIH 19, day 0), the average selectivity index among digits was 61 (out of 100).

In contrast, when only a single multi-contact cuff was examined with its appropriate set of input sources, the results were not as impressive. In the case of the median nerve innervating digits I - IV, the average selectivity index was 38, and for the ulnar nerve innervating digits IV and V the average selectivity was only 9. Thus, by adding more channels and more nerves to the recording scenario, greater selectivity can be achieved.

From recordings performed in NIH 18 on day 0, the selectivity index from all eight channels came out to 59 with selectivities of 32 for the median innervated digits and 10 for the ulnar innervated digits, which was very consistent with results from NIH 19 on day 0.

Mechanical perturbations of digits to test selectivity

To extend the study of multi-contact recordings to more realistic applications, we have also started to apply mechanical perturbations to the digits. A preliminary description of our apparatus was provided in PR#1. Thus far we have applied a simple "contact" stimulus in which a probe is rapidly brought into contact with each digit pad, compresses the pad slightly, and then returns to its initial position.

To date, we have not analyzed the data collected with this method but we have collected and archived considerable data to FM tape and will be starting with this analysis in the next reporting period.

2. Longitudinal IntraFasicular Electrodes

In December of 1996, Dr. Ken Yoshida from U. of Alberta came to the SFU lab to implant Longitudinal IntraFasicular Electrodes (LIFE) into the forelimb nerves of cat NIH 20. Four LIFE pairs were implanted into the median and ulnar nerves, in similar locations as the multi-contact cuffs that were implanted in the previous two cats. With this setup, we can easily compare the performance of the two types of electrode arrays.

The same electrical and mechanical tests have been applied to the LIFE-implanted cat, NIH 20, and the selectivity results have been very good. Over the first month of recordings, the average selectivity index was about 74 when all eight contact sets were used. Looking only at the data from the LIFEs in the median nerve innervating digits I - IV, the average selectivity index was about 57 over the first month of recording. For the ulnar nerve LIFEs, the selectivity index averaged only about 8.

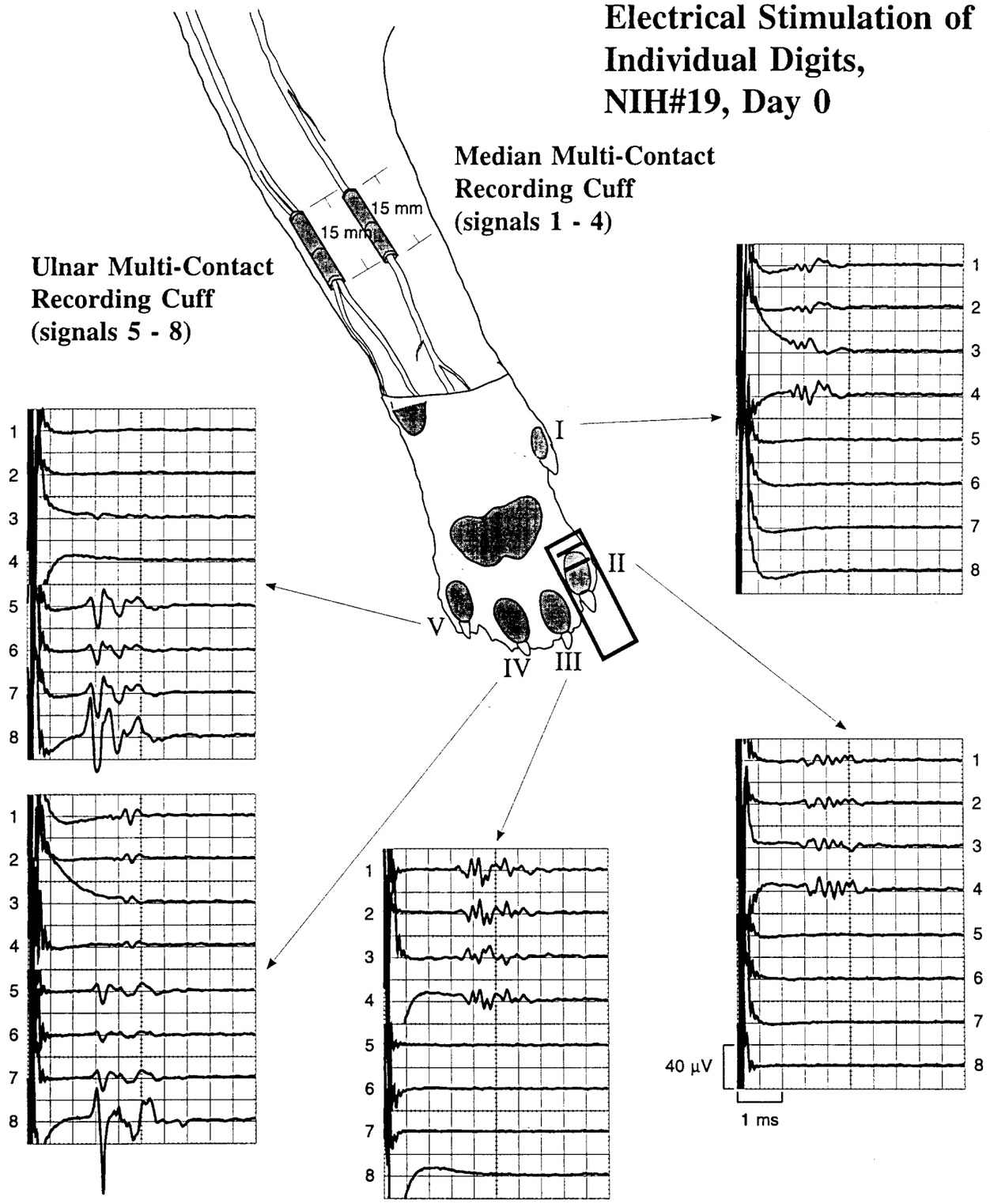


Figure 5: Example of nerve activity recorded on the two multi-contact cuffs after direct electrical stimulation of the digits. NIH 19, Day 0.

E. Long-term stability of Compound Action Potentials and Devices

1. Multi-Contact Cuffs - Subject NIH 18

Subject NIH 18 was implanted with Multi-Contact Cuffs on the Median and Ulnar nerves distal to the elbow. During CAP recordings under anesthesia, the proximal cuff on each nerve was stimulated supramaximally and compound signals were recorded with the four pairs of localized electrodes within the cuff as well as with the set of tripolar, circumferential electrodes sewn into the cuff wall. The circumferential electrodes were of our standard design as reported in previous progress reports.

The conduction latency and amplitude of the circumferential CAPs were used to monitor the status of the whole nerve over the duration of the chronic implant. The amplitudes of the four localized CAPs from each MCC were followed to give an indication of the status of the localized region of nerve as well as the status of the recording electrodes. Impedances were also carefully monitored over the course of the implant.

Table 1 below summarizes the CAP data for subject NIH 18. The CAP amplitude as a percent of the day 0 amplitude is given, as is the status of the nerve, the circumferential and the localized electrodes. The chronic implants are being monitored for at least 180 days. The table gives a summary for the latest day of recording prior to writing this report.

The CAP from the Median nerve in NIH 18 has stabilized at a amplitude higher than day 0 following a change in the CAP shape from polyphasic to triphasic. The localized CAPs are also very stable and suggest that the nerve is healthy and that the MCC's recording characteristics are stable. The impedance data for the Median MCC also suggest stability (data not shown).

Some of the wires to the Ulnar MCC were damaged during the implant surgery, leading to a complete loss of the circumferential Ulnar CAP after day 34. The circumferential electrode impedance increased rapidly during the first few weeks of the implant, and we believe that the wires broke inside the insulation. The localized Ulnar CAPs show mixed results, with CAP amplitudes ranging from 6% to 329% of the day 0 amplitudes. The impedances (data not shown) are generally stable, although they appear to be lower than those seen in the Median MCC.

Table 1: NIH 18, Latest recording day: day 83

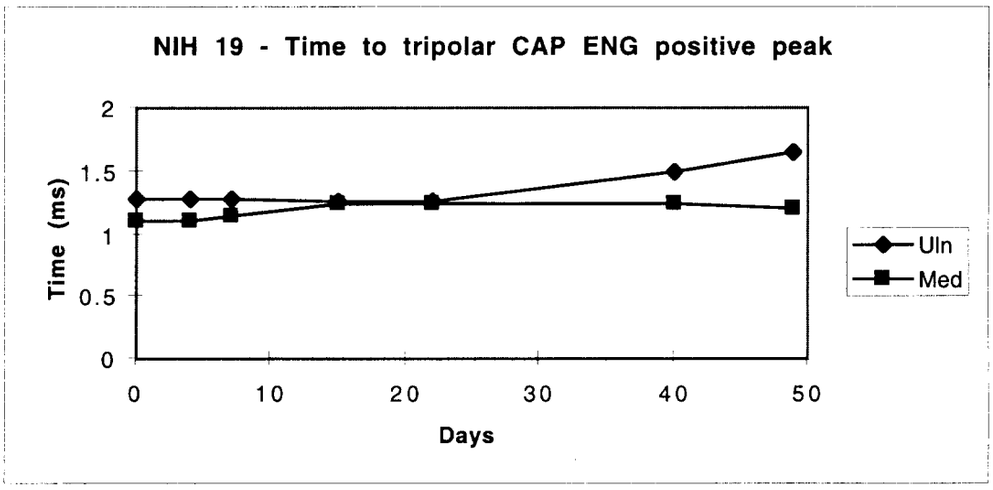
Nerve	CAP amplitude (% of day 0)	Notes
Median (tripolar circumferential) MCC 1v5 2v6 3v7 4v8	217% 123% 156% 113% 116%	Change in CAP shape, polyphasic to triphasic adding up to significantly larger amplitude signal. Slight increase in conduction latency (5%). Localized CAPs are very stable.
Ulnar (tripolar circumferential) MCC 1v5 2v6 3v7 4v8	11% (day 34) 6% 24% 329% 125%	Problems with increasing MCC wire impedances suggesting wires were breaking. Not able to record CAP after day 34. Localized CAPs from 1v5 and 2v6 are slowly decreasing. 4v8 is stable and 3v7 is drastically increasing over the last 35 days.

2. Multi-Contact Cuffs - Subject NIH 19

Subject NIH 19 was implanted with the same devices as NIH 18, with Multi-Contact Cuffs on the Median and Ulnar nerves distal to the elbow. CAP recordings and impedances were also monitored under anesthesia to evaluate the status of the instrumented nerves and the implanted devices.

Figure 6 shows the characteristics of the circumferential CAPs from both the Median and Ulnar nerves over the course of the implant period. The top panel shows the conduction time (time taken between the beginning of the stimulation pulse to the peak of the first positive peak in the compound ENG signal at the distal cuff.) The bottom panel shows the CAP amplitudes after the calibrated amplifier gains were removed.

The circumferential CAP conduction latencies and amplitudes suggest stability for both nerves over the implant period. Some initial fluctuations occurred in the amplitudes in the first few weeks following the implant as the nerve tissues stabilized and as connective tissue enveloped the cuffs and the impedances stabilized (data not shown).



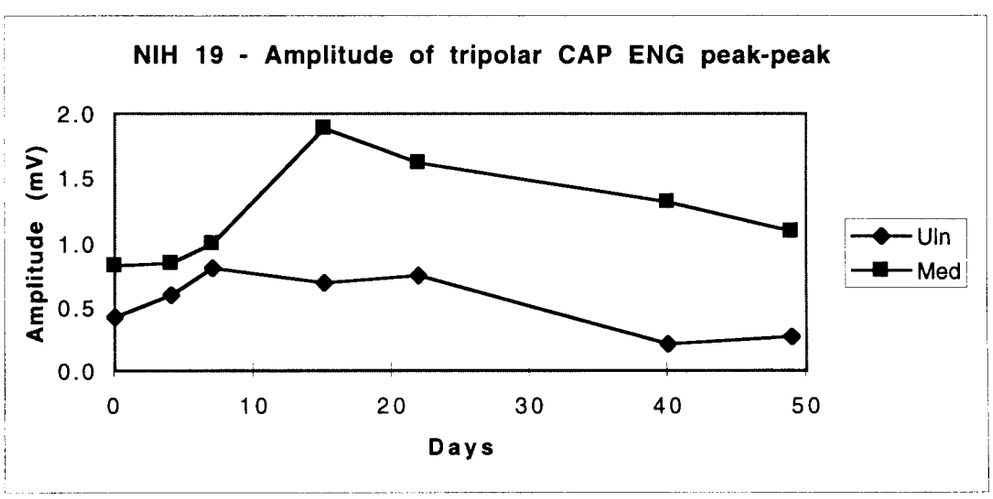


Figure 6: NIH 19 CAP conduction latencies and amplitudes

Figure 7 shows the localized CAPs over the course of the implant period, following the removal of the calibrated amplifier gains. The signals as seen in the MCC are of similar amplitude to the circumferential CAP (in the order of 1 mV).

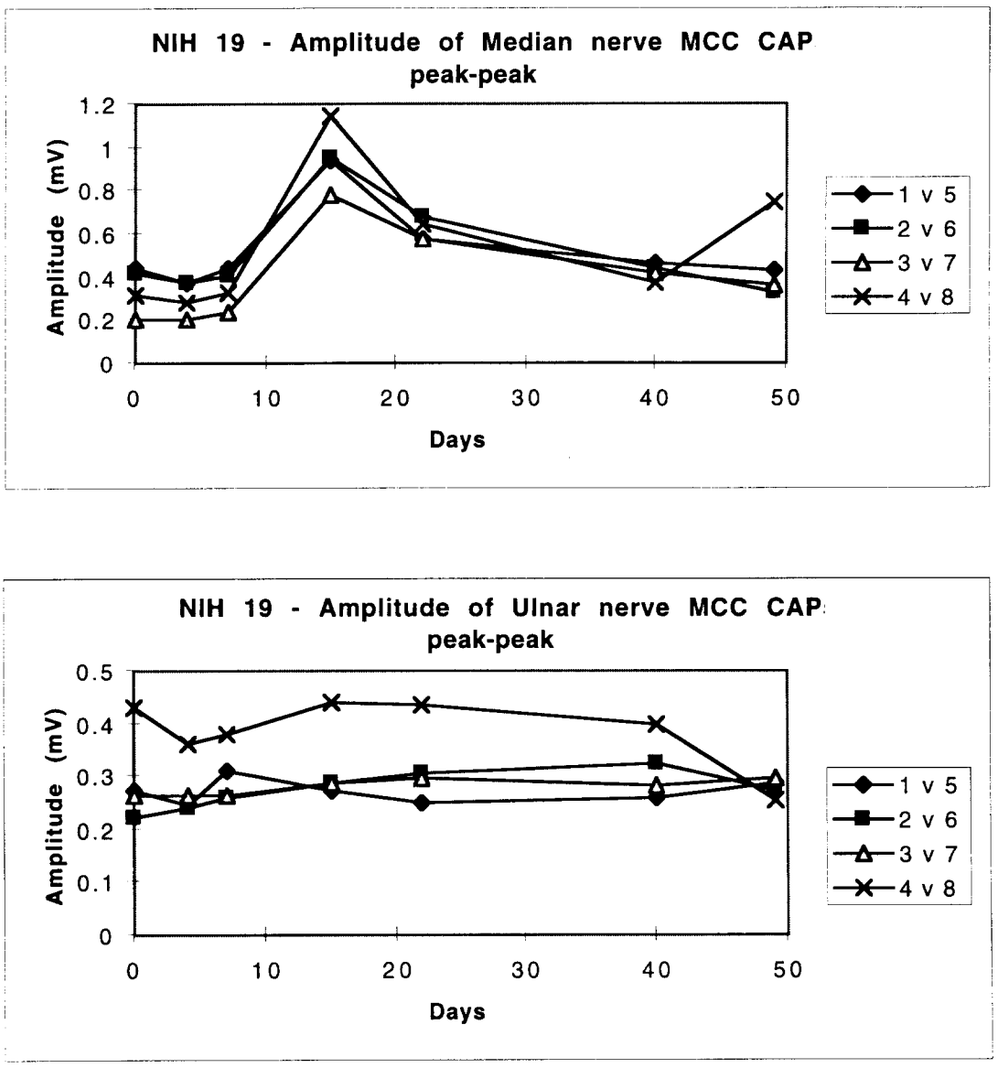


Figure 7: NIH 19 Localized CAP conduction latencies and amplitudes

The top panel in Fig. 7 shows the amplitudes of the localized CAPs from the Median MCC, and the results suggest a high degree of stability over the implant period following a settling period in the first few weeks. The bottom panel shows the amplitudes of the localized CAPs from the Ulnar MCC, which suggest an even higher degree of stability.

Table 2 below summarizes the status of the CAPs from NIH 19 on day 49 as a percentage of day 0.

Table 2: NIH 19, Latest recording day: day 49

Nerve	CAP amplitude (% of day 0)	Notes
Median (tripolar circumferential)	133%	Change in CAP shape, polyphasic to triphasic adding up to larger amplitude signal. Slight increase in conduction time of larger fibres.
MCC		
1v5	97%	
2v6	79%	Localized electrode CAPs are stable or
3v7	182%	increasing (3v7 and 3v8).
4v8	239%	
Ulnar (tripolar circumferential)	66%	Increase in conduction time (11%), leading to spreading of CAP shape and overall decrease of CAP amplitude.
MCC		
1v5	106%	Localized electrode CAPs are stable.
2v6	123%	
3v7	112%	
4v8	59%	

3. Longitudinal IntraFasicular Electrodes - Subject NIH 20

This subject was instrumented with four pairs of LIFEs in each of the Median and Ulnar nerves distal to the elbow. CAP recordings and impedances were monitored under anesthesia to evaluate the status of the instrumented nerves and the implanted devices. Simple tripolar recording cuffs were implanted in the same surgery, distal to the LIFEs such that the distal cuff CAPs indicate the status of the nerve and can be used to evaluate damage resulting from the implants.

Each pair of LIFEs consisted of two fine wires (AM Systems 7750, Teflon-insulated 25 μm Pt-Ir) with 0.5 mm active sites exposed in each wire. The longitudinal electrode separation between the active sites was 2.0 mm. A 50 μm Tungsten needle was used to pass the electrode into an exposed fascicle (from a distal direction) and exit from the same fascicle approximately 0.5 mm proximal to the entry site. The needle was then removed and the fine wires were fixed such that movement of the electrode active sites with respect to the axons surrounding the electrode was restricted. Four pairs of LIFEs were implanted in each of the Median and Ulnar nerves in a radially distributed pattern to approximate the electrode position and pattern in the MCCs.

The LIFE CAPs showed a wide variety of patterns, primarily due to recording from different axons and proximity to these axons. Initial CAP showed that LIFE CAPs were of similar amplitude to the tripolar CAPs and the MCC CAPs, in the order of 1 mV.

Table 3 summarizes the CAP results to date for NIH 20. Both the Median and the Ulnar nerves were quite stable, according to the circumferential CAPs, and all eight pairs of LIFEs also showed good CAP stability. The impedances of the recording nerve cuffs and the LIFEs were also quite stable (data not shown).

Table 3: NIH 20, Latest recording day: day 29

Nerve	CAP amplitude (% of day 0)	Notes
Median (tripolar circumferential)	79%	Slight decrease in conduction velocity of larger fibres. CAP still has original shape and is stable.
LIFEs		
L1	36%	Slight increase in most LIFE CAPs since day 21, but relatively stable.
L2	28%	
L3	24%	
L4	30%	
Ulnar (tripolar circumferential)	84%	Slight decrease in conduction velocity of larger fibres. CAP still has original shape and is stable.
LIFEs		
L1	62%	Slight increase in most LIFE CAPs since day 21, but stable.
L2	18%	
L3	64%	
L4	70%	

The CAP data to date from the three chronically implanted animals suggest that we have achieved stable electrode-nerve interfaces using both approaches. It is encouraging that all the nerves have survived well, the fine LIFE wires have survived the first month of implant, and usable signals can be recorded from all electrodes with the exception of the tripolar signal from the Ulnar nerve in NIH 18. Not surprisingly, the LIFEs in NIH 20, which provide a more intimate interface with stimulated axons inside the nerve, have produced rather more selective recordings than the MCCs during recordings under anesthesia.

We are proceeding with long-term analyses of these two alternative technologies to determine their viability over six months and any trends in selectivity when either electrical or mechanical inputs to digits are used.

IV. Publications and Meetings

A. Publications

1) K.D. Strange and J.A. Hoffer, (1996), "FES state controller using natural sensory feedback", *proc. of 9th Bi. Conf. of CSB*, Vancouver BC, Aug. 21-24, pp. 230-231.

B. Meetings

During this reporting period, we reported on research progress at two conferences:

1) 9th Biennial Conference of the Canadian Society of Biomechanics, Vancouver, August 21-24, 1996. A short paper entitled "FES state controller using natural sensory feedback" authored by K.D Strange and J.A. Hoffer was published in the proceedings. A copy of this paper is included in Appendix A.

2) J.A. Hoffer and K.D. Strange attended the 26th Annual Neural Prostheses Workshop at Bethesda in Oct. 1996. We provided a final report on our progress in our earlier NIH contract and a preliminary report on initial results from our new contract.

V. Plans for the Third Period

During the third reporting period, from Jan. 1, 1997 to April 30, 1997, our objectives will consist of the following:

1) We plan on implanting three more animals for chronic experiments. Two of these animals will be implanted with sets of LIFE electrodes, and the third will be implanted with MCCs. Each animal will be monitored for at least six months, and CAP recordings will be used to evaluate the longevity of the instrumented nerves and the implanted devices.

2) We will continue to assess selectivity of recording during digit electrical stimulation and mechanical perturbation experiments under anesthesia for the three animals currently implanted and for the three future implants.

3) We plan on expanding the single digit manipulator to include tangential perturbations or slips as well as the normal or indenting perturbations studied to date.

4) We plan on expanding the digit manipulator design to include perturbations of all five digits (one at a time) and then possibly multi-modality perturbations (normal and tangential movements) in the same recording sessions.

5) We plan on evaluating the perturbation selectivity data off-line to determine the feasibility of identifying the digit and mode of perturbation based solely on the ENG signals recorded with the LIFEs or the MCCs.

6) We will collect data from the animals during walking on the treadmill. The multi-channel ENG data from the LIFEs and from the MCCs will be evaluated to determine if differences in the signals (and thus the selectivity) can be detected and to determine the reliability and utility of these signals.

7) We will continue our collaboration with Ken Yoshida and Dick Stein by implanting two more animals with LIFEs and collecting data in experiments under anesthesia and during walking on the treadmill.

8) We will begin a collaboration with Aleks Kostov and Brian Andrews by collecting data from the MCCs and virtual sensors during experiments under anesthesia and during walking on the treadmill.

VI. References

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VII. Appendix A: CSB paper

FES STATE CONTROLLER USING NATURAL SENSORY FEEDBACK

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INTRODUCTION

Functional electrical stimulation (FES) is used in clinical systems to return function to patients with extremities paralyzed by spinal cord injury or stroke. Stimulation pulses are applied through surface or implantable electrodes to nerve or muscle tissue below the level of the lesion, resulting in muscle twitch or sustained contraction in paralyzed muscles. FES is currently being implemented to produce standing and walking in paraplegic patients and pinch grip in quadriplegic patients. Closed-loop FES systems may improve the efficacy of clinical systems by including feedback from artificial sensors external to the body or, in a new approach, from natural physiological sensors that remain viable in affected extremities [1,2,3].

In this study, a real-time state controller for FES was developed to test the viability of implementing natural sensory signals from nerve cuffs in the periphery as feedback for closed-loop FES systems.

METHODS

A real-time state controller was designed to control FES of the Palmaris Longus (PalL) muscle in the cat forelimb during walking on the treadmill. The controller used natural sensory signals, recorded with tripolar nerve cuffs implanted on the Median and Superficial Radial nerves of the cat forelimb, as state feedback to detect events in the step cycle such as paw contact and paw lift-off. Figure 1 shows a schematic of the state controller for FES and how threshold analysis of the Radial and Median nerve cuff signals led to accurate information regarding the step cycle.

Figure 1 emphasizes the step-to-step variability during walking which should be accommodated by the state controller when predicting PalL activity. The FES controller was designed to be robust and provide accurate stimulation as required for dynamic operating environments in clinical implementations.

The FES state controller was tested in three conditions: 1) open-loop prediction with no stimulation, 2) closed-loop stimulation of the PalL during normal walking , and 3) closed-loop stimulation of the PalL to return function to the wrist during a Median nerve conduction block. Lidocaine was introduced into a blocking cuff on the Median nerve above the elbow and resulted in a temporary paralysis of Median-innervated forelimb muscles and a greater yield about the wrist (lower wrist elevation) during the stance phase, as shown in Fig. 2.

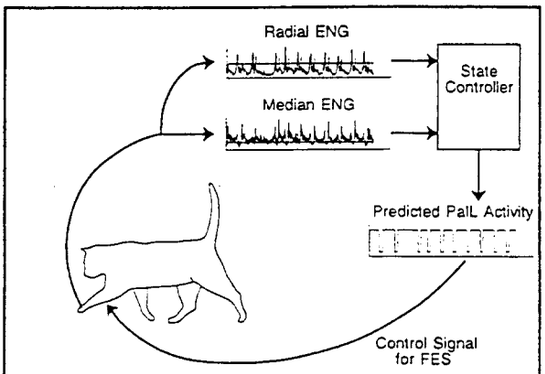

Figure 1: Schematic diagram of closed-loop state controller for functional electrical stimulation in the cat forelimb during walking.

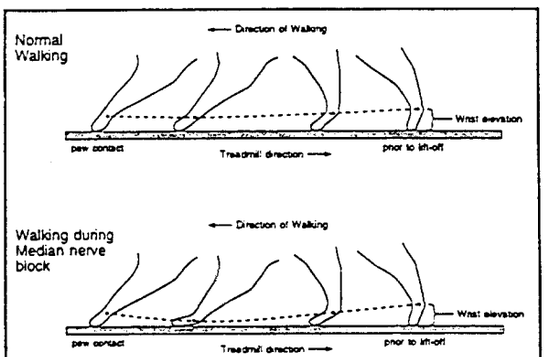

Figure 2: Schematic diagram of effects of Median nerve conduction block. Both panels show the left forelimb in four positions in the stance phase, from paw contact on the left to just prior to lift-off on the right. Dotted line denotes wrist elevation trajectory.

RESULTS

Figure 3 shows a representative result of testing the real-time FES state controller during normal walking on the treadmill (with no stimulation of the PalL). The ENG signals provided accurate information regarding the step cycle which could be reliably detected using threshold analysis to produce a useful stimulation control signal.

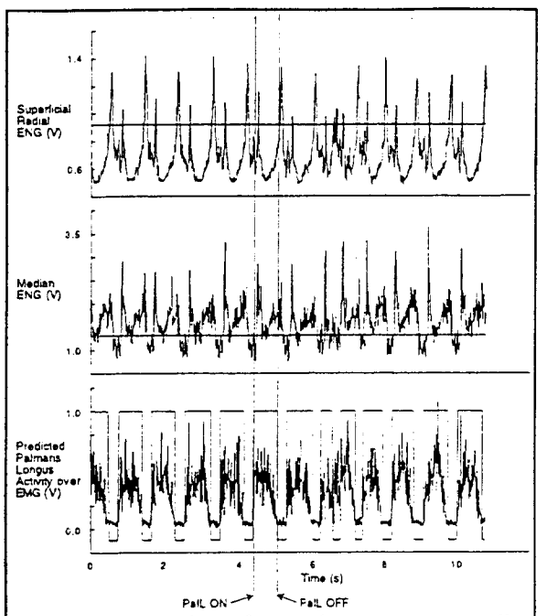

Figure 3: Results of open-loop state controller experiments for level walking at 0.5 m/s (NIH-16, day 62a). In the open-loop experiments, the PalL was not stimulated. The top panel shows the amplified envelope of Superficial Radial ENG supplied to the threshold detector with a threshold of 0.92 V. The middle panel shows the envelope of the Median ENG supplied to the threshold detector with a threshold of 1.32 V. The bottom panel shows the predicted PalL activity superimposed on the recorded PalL EMG.

During experiments where the Median nerve was temporarily blocked, closed-loop stimulation of the PalL resulted in an increase in wrist elevation during the stance phase, as shown in Fig. 4.

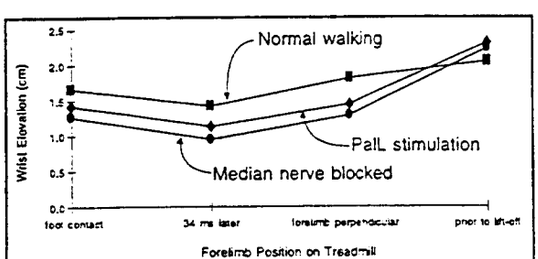

Figure 4: Results of closed-loop state controller experiments for level walking at 0.5 m/s (NIH-16, day 78), showing normal walking (■), walking with Median nerve conduction block (●), and walking with conduction block and superimposed FES of PalL (◆). Each of three traces represents average wrist elevation for 10 consecutive steps.

DISCUSSION

The nerve cuff signals from cat forelimb cutaneous nerves showed highly repeatable modulations during the step cycle for a range of walking conditions (treadmill speeds and slopes) as well as over time (up to 300 days for one cat). The repeatability of the neural signals allowed for reliable detection of neural activity peaks related to events in the step cycle using simple threshold analysis. Nerve signal thresholds were set at the beginning of each recording session and then held constant.

The state controller output closely matched the timing of naturally occurring PalL EMG during normal walking with no stimulation. The resulting PalL stimulation control signal was used to stimulate the muscle with the proper timing while effectively blanking out stimulus artifacts from the nerve cuff signals. During Median nerve conduction block, closed-loop stimulation of the PalL during the stance phase produced a measurable improvement in wrist elevation over the blocked nerve condition.

The accurate, reliable results obtained by using sensory nerve signals to control stimulation in a variety of walking conditions in the cat suggest that nerve cuff signals may provide sensory feedback applicable for clinical neural prostheses applications.

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